REMARKS

Claims 1-5 currently appear in this application. The Office Action of March 23, 2006, has been carefully studied. These claims define novel and unobvious subject matter under Sections 102 and 103 of 35 U.S.C., and therefore should be allowed. Applicant respectfully requests favorable reconsideration, entry of the present amendment, and formal allowance of the claims.

Claims 1-4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Reich et al., U.S. 5,288,489 in view of Chan et al., U.S. 6,566,098. The Examiner's position is that hepatocyte growth factor (HGF) resembles plasminogen in that it possesses characteristic kringle domains so that the mode or separating Kringle fragments disclosed in Chan should be applicable to plasminogen.

This rejection is respectfully traversed. It is respectfully submitted that one of ordinary skill in the art would not be motivated to combine the teachings of Reich with that of Chan. There is neither disclosure nor suggestion in any of Reich or of Chan that would lead one of ordinary skill in the art to reasonably consider combining these two patents.

Reich relates to treating and preventing thrombotic disorders, *i.e.*, fibrinolysis or fibrinogenolysis treatment,

which includes the parenteral introduction of human or mammalian plasmin or mini- or micro-plasmin into the body of a patient. In preferred embodiments, fibrinolytical/ fibrinogenolytical plasminogen is converted to fibrinolytically/fibrinogenolytically active plasmin. In one embodiment of preparing a substrate of mini-plasminogen, Reich discloses the fragment that encompasses the Lys-Lysine binding site I as claimed herein.

Chan relates to a DNA encoding recombinant HGF variants, *i.e.*, a novel truncated form of HGF which specifically antagonizes the activity of HGF, such as HGF/NK2, that includes the N-terminal and the first two kringle domains of HGF and that specifically inhibits HGF-induced mitogenesis, as well as a novel truncated form of HGF which is a partial agonist, such as HGF/NK1, comprising the N-terminal and the first kringle domain of HGF (column 7, line 67 to column 8, line 3 and column 8, lines 30-32). Chan describes how HGF has hormone-like activity and is released in response to partial hepatectormy and liver injury, and is presumed to be an important mediator of liver regeneration (column 1, lines 24-27). HGF is known to be capable of specifically binding to the c-met oncogene product and to have six domains: amino terminal, Kringle 1, Kringle 2, Kringle 3, Kringle 4, and some protease domains (column 7, lines 18-24). Chan also describes

that the ubiquitous expression of HGF by stromal fibroblasts and demonstrated ability to stimulate DNA synthesis in melanocytes and endothelial cells as well as epithelial cells suggests that this factor plays a role in paracrine regulation of cell growth as well (column 1, lines 30-34). Chan also discloses a method for producing substantially pure HGF variant by heparin affinity chromatography which involves heparin treatment using heparin supports so as to form a heparin-HGF variant complex, from which the HGF variant is then dissociated.

Despite some structural resemblance between plasminogen and HGF, they are functionally utterly distinct proteins both biologically, biochemically, and clinically. Although both Reich and Chan relate to the field of medical or life science, there is nothing in either Reich or Chan that would lead one skilled in the art to assume that plasminogen and HGF can be treated the same way. This is further verified by the fact that Chan contains enabling disclosure only for the specific HGF variants, namely, HGF/NK2 that includes the N-terminal and the first two kringle domains of HGF, and HGF/NK1. Comprising the N-terminal and the first kringle domain of HGF, both of which comprise at most the first **two** kringle domains. In contrast thereto, the Lys-Lys binding site as claimed herein is a plasminogen fragment consisting of

Kringle 1 to Kringle 3 of a human plasminogen, namely, **three** kringle domains. Finally, it should be noted that the claimed invention **lies in the Lys-Lys binding site I, *i.e.*, the specific plasminogen fragment per se that has properties (a) to (d) as claimed herein.** The fact that the fragment is prepared by heparin affinity chromatography is not an essential feature. Neither Reich nor Chan teaches properties (a) to (d) possessed by the Lys-Lys binding site I of the fragment claimed herein. Therefore, there is no reason for one of ordinary skill in the art to combine the teachings of Reich with the teachings of Chan.

Thus, even if the starting material of Reich is the same as applicants' starting material, and if arguably the same mode of separation would yield the same product as claimed herein, as suggested by the Examiner, Reich does not teach the fragments have been subjected to heparin affinity chromatography for selecting heparin-binding fractions. The fragments claimed herein have **three** kringles, which is not shown or suggested in either Chan or Reich. There is nothing in either Chan or Reich that would motivate one skilled in the art to prepare the fragment claimed herein.

In view of the above, it is respectfully submitted that the claims are now in condition for allowance, and favorable action thereon is earnestly solicited.

Respectfully submitted,

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